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Lowering heart rate with an optimised breathing protocol for prospectively ECG-triggered CT coronary angiography

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Abstract: The breath-hold level to best reduce heart rate for CTCA should be individually assessed prior to scanning because a mean heart rate reduction of 5 bpm can be achieved.

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Lowering Heart Rate with an Optimized Breathing Protocol for Prospectively ECG-Triggered CT Coronary Angiography

Running Head: Optimized Breathing Protocol for Cardiac CT

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Lowering Heart Rate with an Optimized Breathing Protocol for Prospectively ECG-Triggered CT Coronary Angiography

Abstract

Objective: To prospectively characterize the effect of the level of breath-hold on heart rate in computed tomography coronary angiography (CTCA) with prospective electrocardiogram (ECG)-triggering and its impact on coronary artery attenuation.

Materials and Methods: Two-hundred-sixty patients (86 women, mean age 59 ± 11 years) underwent 64-slice CTCA using prospective ECG-triggering. Prior to CTCA heart rates were recorded during 15 seconds of breath-hold in three different levels of inspiration (normal, intermediate and deep). The inspiration level with the lowest heart rate was chosen for actual CTCA scanning. Coronary artery attenuation was measured, and the presence of backflow of contrast material into the inferior vena cava (IVC) (as an indicator of increased intrathoracic pressure) was recorded.

Results: Mean heart rate at breath-hold was significantly different for the three inspiration levels (normal: 60 ± 8 bpm, intermediate: 59 ± 8 bpm, deep: 57 ± 7 bpm; $P < 0.001$). The maximum heart rate reduction in each patient at breath-hold averaged 5.3 ± 5.1 bpm, and was observed at normal inspiration depth in 23 patients (9%), at intermediate inspiration depth in 102 patients (39%) and at deep inspiration in 135 patients (52%).

Overall there was no association between the level of breath-hold and coronary vessel attenuation ($P = n.s$). However, backflow of contrast material into the IVC ($n = 26$) was found predominantly at deep inspiration levels ($P < 0.001$), and when it occurred, it was associated with reduced coronary attenuation compared to patients with no backflow ($P < 0.05$).

Conclusions: The breath-hold level best reducing heart rate for CTCA should be individually assessed prior to scanning, as a mean heart rate reduction of 5 bpm can be achieved.

Keywords: breath-hold, heart rate, coronary artery attenuation, computed tomography coronary angiography, prospective ECG-triggering, step-and-shoot

Introduction

Low dose computed tomography coronary angiography (CTCA) with prospective electrocardiogram (ECG)-triggering has recently been introduced [1] and shown to offer a tremendous reduction of radiation dose [2-8], making its widespread clinical use feasible. Scanning in CTCA with prospective ECG-triggering is exclusively performed during a short phase in diastole, called “diastasis”. The new technique appears to be more prone to artifacts caused by coronary motion, especially in higher heart rates, as “diastasis” unproportionally shortens with increasing heart rates [9], and the length of “diastasis” will become shorter than the time required for image acquisition when heart rates exceed a certain threshold. Furthermore, when low dose CTCA with prospective ECG-triggering is performed with the smallest possible acquisition window to grant the lowest possible radiation dose, it does not permit image reconstruction in other phases of the cardiac cycle to compensate for possibly reduced image quality. Therefore, an aggressive reduction of heart rate with beta blockers below a target heart rate of 63 bpm appears to be a prerequisite for low-dose CTCA [2, 10].

CTCA is generally performed during patient’s breath-hold to avoid motion artifacts caused by movement of the thorax during image acquisition. However, the breath-hold and particularly the level (or depth) of breath-hold impacts heart rate [11]. Generally, heart rate is lowest at full vital capacity (deep inspiration) and highest at residual volume (normal inspiration) [11]. However, other factors such as intrapleural and intrathoracic pressure, and neural reflexes also determine heart rate during breath-hold [11], and lowest heart rates are therefore not always reached at deep inspiration level during breath-hold. Furthermore during CTCA, very deep inspiration for breath-hold may lead to an increased intrathoracic pressure (Valsalva effect), which on its part may impair contrast material flow from the arm veins to the coronary

arteries, and thus, cause reduced coronary artery attenuation and decreased image quality.

Accordingly, the purpose of this study was twofold: to describe and characterize the effect of breath-hold on heart rate, and on coronary artery attenuation in CTCA with prospective ECG-triggering.

Materials and Methods

Patients

Three-hundred-two consecutive patients with suspected (n=274) or known (n=28) CAD referred to CTCA were prospectively enrolled in the present study if none of the following exclusion criteria were present: hypersensitivity to iodinated contrast material, renal insufficiency (creatinine levels $>150 \mu\text{mol/L}$, or $>1.7\text{mg/dl}$), non-sinus rhythm, or heart rates >63 bpm despite beta-blocker medication.

The study protocol was approved by the institutional review board, written informed consent was obtained.

CT data acquisition and post-processing

To obtain the lowest possible heart rates for the CTCA examination we tried to create a calm and quite atmosphere during patient preparation. Patients were thoroughly instructed about the course of events during the examination. To determine the inspiration level with the lowest heart rate, 3 different breathing commands were practiced repetitively under heart rate monitoring and recording prior to scanning: First, patients were asked to breath normally and stop breathing after normal inspiration; then patients were asked to deeply inspire and hold their breath, and finally patients were asked to find a level of inspiration in between the first two (normal and deep inspiration). Breath-hold was performed for 15 seconds (according to the maximum scan duration) in each inspiration depth with at least 30 seconds of normal breathing in between two different commands.

If heart rates were >63 bpm during breath-hold at the inspiration depth with the lowest heart rate, 2.5 mg intravenous metoprolol (Beloc, AstraZeneca, London, UK) were administered and all breathing commands were repeated. Intravenous beta blocker administration and breathing commands were repeated up to 8 times

(maximum 20 mg of metoprolol). If the target heart rate ≤ 63 bpm could not be reached scanning was not performed. A single dose of 2.5 mg isosorbiddinitrate sublingual (Isoket, Schwarz Pharma, Monheim, Germany) was administered 2 min prior to the scan in all patients.

For CTCA, a body mass index (BMI)-adapted contrast material protocol was applied: BMI: $<17.5 \text{ kg/m}^2$, 50ml of iodixanol (Visipaque 320, 320 mg/mL, GE Healthcare, Buckinghamshire, UK) at 4.0 ml/sec; $17.5\text{-}22.4 \text{ kg/m}^2$: 55 ml at 4.0 ml/sec; $22.5\text{-}24.9 \text{ kg/m}^2$: 65 ml at 4.0 ml/sec; $25.0\text{-}27.4 \text{ kg/m}^2$: 80 ml at 4.5 ml/sec; $27.5\text{-}29.9 \text{ kg/m}^2$: 80ml at 5.0 ml/sec; $30.0\text{-}34.9 \text{ kg/m}^2$: 85 ml at 5.0 ml/sec; $35.0\text{-}40.0 \text{ kg/m}^2$: 95ml at 5.0 ml/sec; $>40 \text{ kg/m}^2$: 105 ml at 5.0 ml/sec . Contrast material was injected into an antecubital vein via an 18-gauge catheter and was followed by 50 ml saline solution. Bolus tracking was performed with a region of interest placed into the ascending aorta, and image acquisition was started 4 s after the signal density reached a threshold of 120 Hounsfield units (HU).

All CTCA examinations were performed with a LightSpeed VCT XT scanner (GE Healthcare) and with prospective ECG-triggering using the following scanning parameters: slice acquisition $64 \times 0.625 \text{ mm}$, smallest x-ray window (only 75% of the RR-cycle), z-coverage 40 mm with an increment of 35 mm, gantry rotation time 350 ms, BMI adapted tube voltage (100 kV: BMI $<25 \text{ kg/m}^2$, 120 kV: BMI $\geq 25 \text{ kg/m}^2$) and effective tube-current (450 mA: BMI $<22.4 \text{ kg/m}^2$, 500 mA: BMI $22.5\text{-}24.9 \text{ kg/m}^2$, 550 mA: BMI $25\text{-}27.4 \text{ kg/m}^2$, 600 mA: BMI $27.5\text{-}29.9 \text{ kg/m}^2$, 650 mA: BMI $30\text{-}40 \text{ kg/m}^2$, 700 mA: BMI $>40 \text{ kg/m}^2$). Scanning was performed from below the tracheal bifurcation to the diaphragm, choosing 3 to 5 scan blocks (field of view 11 to 18 cm). All images were transferred to an external workstation (AW 4.4, GE Healthcare).

CT image analysis

Measurements of vessel attenuation were performed in the proximal right coronary artery (RCA) and the left main artery (LMA) by one experienced reader (L.H.), who drew regions of interest as large as possible, carefully avoiding calcifications, plaques, and stenoses as previously described [12, 13]. The mean from both measurements was calculated and defined as coronary vessel attenuation.

Furthermore, two readers (L.H. and B.H) in consensus determined the presence of backflow of contrast material into the inferior vena cava. If back flow was present (**Fig. 1**), it was graded semiquantitatively on a 4-point Likert scale (1: very low, 2: low, 3: intermediate, 4: high). The determination of backflow of contrast material into the inferior vena cava served to visualize increased intrathoracic pressure (Valsava effect).

Statistical analysis

Quantitative variables were expressed as mean \pm standard deviation and categorical variables as frequencies, or percentages.

Differences between the three groups (level of inspiration) were determined by univariate analyses of variances (ANOVA) for heart rate and coronary vessel attenuation and by χ^2 -tests for the presence of contrast material in the inferior vena cava. Pearson linear correlation analysis was performed to determine the relation of interindividual heart rate variability with age and BMI. Mann-Whitney-U-tests were used to determine differences in coronary vessel attenuation in patient groups without or with the presence of backflow of contrast material into the inferior vena cava. The relationship between the grade of the backflow and coronary vessel attenuation was analyzed with Spearman rank-order correlation coefficients.

A *P*-value of <0.05 was considered to indicate statistical significance. SPSS

software (SPSS 15.0, Chicago, ILL, USA) was used for statistical testing.

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Results

CTCA was successfully performed in 281 of 302 consecutive patients; 21 patients were excluded because CTCA was not feasible due to non-sinus rhythm (n=8), because heart rate could not be sufficiently reduced with beta-blocker medication (n=12), or because of elevated creatinine levels (n=1). Another 21 patients were retrospectively excluded because of language barriers forbidding three different breathing commands (n=7) or because heart rates were not properly recorded (n=14). Demographics of the final study population (n=260) are given in table 1.

Forty-two of 260 patients (16%) were on beta blocker medication as part of their baseline medication; additional intravenous beta blockers were administered for heart rate control prior to CTCA in 188 patients (72%).

Heart rate and inspiration levels

The mean heart rate at the three inspiration levels during breath-hold (normal, intermediate and deep) showed little but significant variation (60 ± 8 bpm, 59 ± 8 bpm, 57 ± 7 bpm; $P < 0.001$; **Fig. 2A**). Mean heart rate at breath-hold was significantly different for the three inspiration levels (normal: 60 ± 8 bpm, intermediate: 59 ± 8 bpm, deep: 57 ± 7 bpm; $P < 0.001$). The maximum heart rate reduction in each patient at breath-hold averaged 5.3 ± 5.1 bpm, and was observed at normal inspiration depth in 23 patients (9%), at intermediate inspiration depth in 102 patients (39%) and at deep inspiration in 135 patients (52%).

The mean interindividual heart rate variability during breath-hold was associated with the patient's age ($r = -0.22$; $P < 0.001$), while there was no such association with the BMI ($r = 0.01$; $P = \text{n.s.}$).

Coronary vessel attenuation and inspiration levels

Mean attenuation was 396 ± 83 HU (range 190 to 686 HU) in the LMA and 378 ± 78 HU (range 140 to 634 HU) in the RCA, resulting in a mean coronary vessel attenuation of 387 ± 77 HU (range 178 to 626 HU) (three measurements in the proximal RCA were not feasible due to one vessel occlusion and two severe motion artifacts).

Overall, there was no association between the levels of breath-hold and coronary vessel attenuation ($P=n.s.$, **Fig. 2B**).

However, backflow of contrast material into the inferior vena cava occurred in 26 patients (10%) and was associated with the level of breath-hold ($P<0.001$; normal $n=1$, intermediate $n=7$ and deep $n=18$). The presence of backflow of contrast material into the inferior vena cava was associated with reduced coronary vessel attenuation ($P<0.05$, **Fig. 3A**), while the grade of the backflow was not ($P=n.s.$, **Fig. 3B**). Furthermore, backflow was not related to the amount or flow rate of contrast material ($P=n.s.$).

Discussion

Low heart rates are a prerequisite for diagnostic image quality in CTCA with prospective ECG-triggering [2]. Our study adds to the previous knowledge [1-8] on CTCA with prospective ECG-triggering the following results: (i) the heart rate can be reduced by about 5 bpm by choosing the adequate level of breath-hold for CTCA in each patient individually (ii) the maximum heart rate reduction during breath-hold can be obtained at normal inspiration levels in 9% of patients, at intermediate inspiration levels in 39% of patients, and at deep inspiration in 52% of patients (iii) coronary vessel attenuation is not influenced by the level of breath-hold and (iv) in 10% of patient backflow of contrast material into the inferior vena cava (as an indicator of increased intrathoracic pressure) can be observed, and if backflow occurs, coronary vessel attenuation is reduced and correlated with the level of breath-hold.

In CTCA with prospective ECG-triggering scanning is exclusively performed during a short phase in diastole, called “diastasis”, in which coronary motion velocities are relatively low [9, 14, 15]. This phase of the cardiac cycle unproportionally shortens with increasing heart rates [9], making motion-artifacts-free imaging more unlikely, as the minimum time required for image acquisition (i. e. half a rotation of the x-ray tube, about 175 ms) will become shorter than the duration of “diastasis”. Therefore, aggressive reduction of heart rate with beta blockers is required for low-dose CTCA with prospective ECG-triggering. Different groups have concordantly reported the administration of high doses of beta-blockers [2-7], but nonetheless a certain percentage of patients could not be scanned, as heart rate reduction with beta blockers was not sufficient [2-8].

Zhang and colleagues [16] could demonstrate that heart rates during breath-hold in CTCA are lower as compared to normal breathing prior to scanning. However,

1 reductions in heart rate during breath-hold are proportional to initial lung volumes
2 [11], with the greatest reduction in heart rate occurring when breath-hold is
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4 performed at deep inspiration, and the variations in extent of breath-hold altering the
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6 magnitude of the heart rate reductions [11]. The latter is well in line with the results of
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8 the present study, showing the lowest mean heart rates at deep inspiration during
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10 breath-hold. However, in a large proportion of patients in our study population, lowest
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12 heart rates were not only found at deep inspiration level during breath-hold, but at
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14 normal (9%) or intermediate (39%) inspiration level. This demonstrates that the
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16 physiologic impact of breathing on heart rate can be further exploited by introducing a
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18 routine clinical protocol for CTCA, in which the inspiration level for breath-hold is
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20 determined in each individual patient prior to CTCA scanning. With this a reduction of
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22 the mean heart rate of about 5 bpm was demonstrated (especially in younger
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24 patients), possibly allowing a reduction of the required amount of beta blockers
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26 and/or an improvement of the image quality in CTCA with prospective ECG-
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28 triggering.
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39 A contrary effect on image quality in CTCA associated with deep inspiration
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41 during breath-hold may be associated with the increased intrathoracic pressure
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43 (Valsalva effect), which may impair arterial vessel attenuation [17]. Increased
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45 intrathoracic pressure may hamper contrast material flow from the arm veins to the
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47 coronary arteries, or lead to back flow of contrast material into the inferior vena cava
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49 from the right atrium. In the present study we could demonstrate that backflow of
50
51 contrast material into the inferior vena cava occurred in 10% of our patients and was
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53 associated with the level of breath-hold and with reduced coronary vessel
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55 attenuation. Controversially, other authors have hypothesized that an increased
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57 return of venous unenhanced blood from the inferior vena cava during deep
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1 inspiration may cause dilution of the contrast material bolus and hence decrease
2 artery attenuation [17]. As no flow measurements are feasible in CTCA imaging, we
3 cannot exclude that the latter influenced the attenuation measurements in the
4 present study, which represents a limitation of our work. However, we presume that
5 the physiologic effect of intrathoracic pressure differences caused by different
6 inspiration levels during breath-hold is negligible in CTCA with prospective ECG-
7 triggering, as no significant relation was observed in our large study cohort.
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19 In conclusion, the breath-hold level best reducing heart rate for CTCA should
20 be individually assessed prior to scanning, as a mean heart rate reduction of 5 bpm
21 can be achieved. The effect on coronary artery attenuation by the level of breath-hold
22 appears negligible.
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Figure legends

Fig. 1:

Volume rendered reconstruction demonstrates remaining contrast material in the superior vena cava (arrow heads in A and B) and back flow of contrast material from the right atrium into the inferior vena cava (arrows in A, C, and D) in a patient who inspired deeply for breath-hold during CTCA image acquisition.

Fig. 2:

Box plots demonstrate mean heart rate in all 260 patients during breath-hold at three different depths of inspiration: normal, intermediate and deep (A). Mean heart is significantly lower during deep inspiration ($P < 0.001$). Box plots in B demonstrate the mean coronary vessel attenuation, with no relation to the depth of breath-hold, which was chosen for each patient individually to obtain the lowest possible heart rate during CTCA. Box = 1st to 3rd quartiles, mid line = median, whiskers = minimum and maximum values, circle = mild outlier, asterix = extreme outlier.

Fig. 3:

Box plots demonstrate significantly lower mean coronary vessel attenuation in patients in whom backflow of contrast material into the inferior vena cava from the right atrium occurred (A, $P < 0.05$). In these 26 patients mean coronary vessel attenuation is not significantly associated with the visually graded degree of backflow (B). Box = 1st to 3rd quartiles, mid line = median, whiskers = minimum and maximum values, circle = mild outlier.

Table 1. Patient demographics

Number of patients	260
Age in years (mean \pm SD)	59 \pm 11
Female gender	86
Male gender	174
Body mass index in kg/m ² (mean \pm SD)	26 \pm 5
Weight in kg	78 \pm 15
Height in cm	172 \pm 9
Heart rate in bpm	56 \pm 6
Known CAD	26
Previous infarction	12
Previous stent placement	14
Coronary risk factors	
Smokers	89
Hypertension	131
Diabetes	29
Positive family history	110
Dyslipidemia	116

Figure 1
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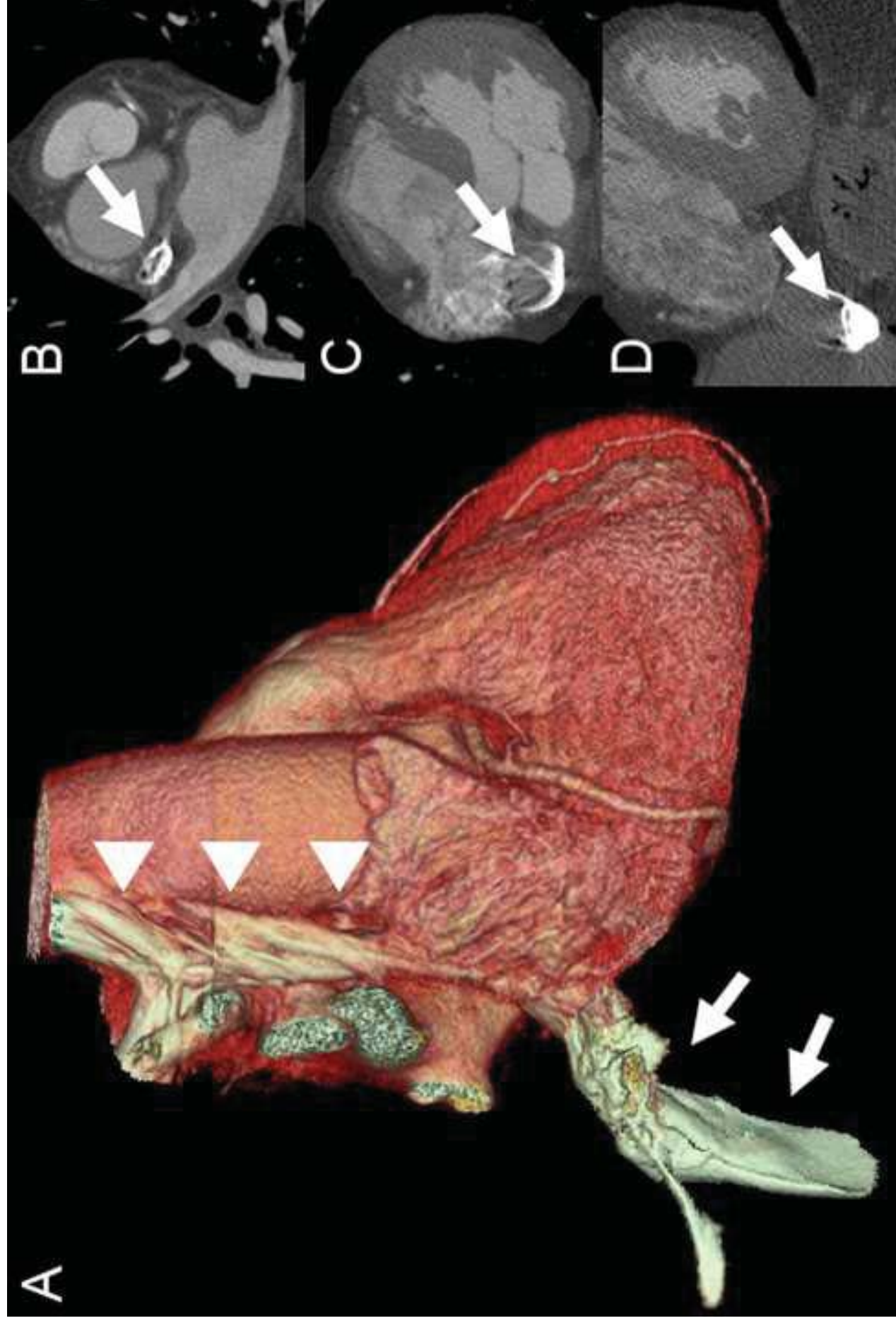


Figure 2

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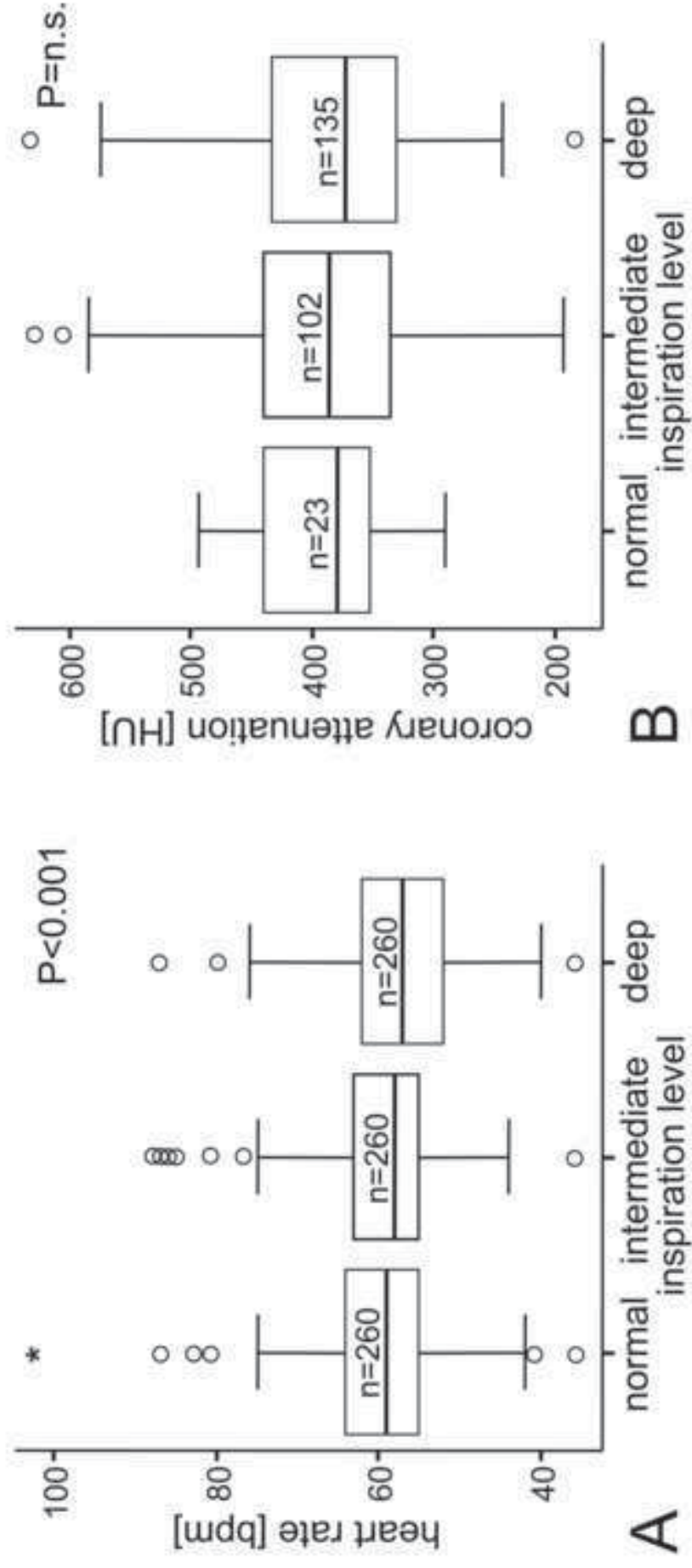


Figure 3

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